CONCLUSION

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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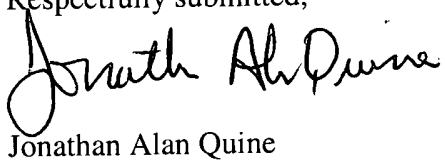
Respectfully submitted,



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APPENDIX A

"MARKED UP" CLAIMS ILLUSTRATING THE AMENDMENTS MADE TO THE CLAIMS OF 09/760,010 WITH ENTRY OF THIS AMENDMENT

1 **(AMENDED).** A device or **[integrated]** system, comprising: a physical or logical array of reaction mixtures, each reaction mixture comprising one or more shuffled or mutagenized nucleic acids or one or more transcribed shuffled or transcribed mutagenized nucleic acids and one or more in vitro translation reagents.

2 **(AMENDED).** The device or **[integrated]** system of claim 1, further comprising a duplicate of the physical or logical array.

3 **(AMENDED).** The device or **[integrated]** system of claim 1, further comprising a bar-code based sample tracking module, which module comprises a bar code reader and a computer readable database comprising at least one entry for at least one array or at least one array member, which entry is corresponded to at least one bar code.

4 **(AMENDED).** The device or **[integrated]** system of claim 1, further a long term storage device comprising of one or more of: a refrigerator; an electrically powered cooling device; a device capable of maintaining a temperature of < 0 C; a freezer; a device which uses liquid nitrogen or liquid helium for cooling storing or freezing samples, a container comprising wet or dry ice, a constant temperature and/or constant humidity chamber or incubator; or an automated sample storage or retrieval unit.

5 **(AMENDED).** The device or **[integrated]** system of claim 4, further comprising one or more modules for moving arrays or array members into the long term storage device.

6 **(AMENDED).** The device or **[integrated]** system of claim 1, further comprising a copy array comprising a copy of each of a plurality of members of the one or more shuffled or mutagenized nucleic acids in a physically or logically accessible arrangement of the members.

7 (AMENDED). The device or **[integrated]** system of claim 1, wherein a plurality of the reaction mixtures further comprise one or more translation products or one or more transcription products, or both one or more translation products and one or more transcription products.

8 (AMENDED). The device or **[integrated]** system of claim 1, wherein the array of reaction mixtures comprises a solid phase, liquid phase or mixed phase array of one or more of: the one or more shuffled nucleic acids, the one or more transcribed shuffled nucleic acids, or the one or more in vitro translation reagents.

9 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more shuffled nucleic acids are homologous.

10 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more transcribed shuffled nucleic acid is an mRNA.

11 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more in vitro translation reagents comprise one or more of: a reticulocyte lysate, a rabbit reticulocyte lysate, a canine microsome translation mixture, a wheat germ in vitro translation (IVT) mixture, or an *E coli* lysate.

12 (AMENDED). The device or **[integrated]** system of claim 1, further comprising one or more in vitro transcription reagents.

13 (AMENDED). The device or system of claim 12, wherein the in vitro transcription reagents comprises one or more of: an *E. coli* lysate, an *E. coli* extract, an *E coli* s20 extract, a canine microsome system, a HeLa nuclear extract in vitro transcription component, an SP6 polymerase, a T3 polymerase or a T7 RNA polymerase

14 (AMENDED). The device or **[integrated]** system of claim 1, further comprising a nucleic acid shuffling or mutagenesis module, which nucleic acid shuffling or mutagenesis module accepts input nucleic acids or character strings corresponding to input nucleic acids and manipulates the input nucleic acids or the character strings corresponding to input nucleic acids to produce output nucleic acids, which output

nucleic acids comprise the one or more shuffled or mutagenized nucleic acids in the reaction mixture array.

15 (AMENDED). The device or **[integrated]** system of claim 14, wherein the output nucleic acids comprise one or more sequence which controls transcription or translation.

16 (AMENDED). The device or **[integrated]** system of claim 14, wherein the nucleic acid shuffling or mutagenesis module comprises a DNA shuffling module, which DNA module accepts input DNAs or character strings corresponding to input DNAs and manipulates the input DNAs or the character strings corresponding to input DNAs to produce output DNAs, which output DNAs comprise the one or more shuffled DNAs in the reaction mixture array.

17 (AMENDED). The device or **[integrated]** system of claim 1, wherein the nucleic acid shuffling or mutagenesis module is preceded by a module which allows overlapping synthetic oligonucleotides to be first assembled into oligonucleotide multimers or functional open reading frames prior to entering the mutagenesis or shuffling module.

18 (AMENDED). The device or **[integrated]** system of claim 14, wherein one or more module comprises or is operatively linked to a thermocycling device.

19 (AMENDED). The device or **[integrated]** system of claim 14, wherein the nucleic acid shuffling or mutagenesis module comprises a mutagenesis module, which mutagenesis module mutagenizes the DNA.

20 (AMENDED). The device or **[integrated]** system of claim 14, wherein the nucleic acid shuffling or mutagenesis module fragments the input nucleic acids to produce nucleic acid fragments, or wherein the input nucleic acids comprises cleaved or synthetic nucleic acid fragments.

21 (AMENDED). The device or **[integrated]** system of claim 14, wherein the shuffling or mutagenesis module is mechanically, electronically, robotically or fluidically coupled to at least one other array operation module.

22 (AMENDED). The device or **[integrated]** system of claim 14, wherein, the nucleic acid shuffling or mutagenesis module performs one or more of: StEP PCR, uracil incorporation or chain termination.

23 (AMENDED). The device or **[integrated]** system of claim 14, or 20, wherein the nucleic acid shuffling module comprises an identification portion, which identification portion identifies one or more nucleic acid portion or subportion.

24 (AMENDED). The device or **[integrated]** system of claim 14 or 20, wherein the nucleic acid shuffling module comprises a fragment length purification portion, which fragment length purification portion purifies selected length fragments of the nucleic acid fragments.

25 (AMENDED). The device or **[integrated]** system of claim 20, wherein the nucleic acid shuffling module permits hybridization of the nucleic acid fragments and wherein the nucleic acid shuffling module comprises a polymerase which elongates the hybridized nucleic acid.

26 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module combines one or more translation or transcription control sequence into the resulting elongated nucleic acid.

27 (AMENDED). The device or **[integrated]** system of claim 26, wherein the one or more translation or transcription control sequence is combined into the resulting elongated nucleic acid using the polymerase, or a ligase, or both the polymerase and the ligase.

28 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module separates, identifies, purifies or immobilizes the resulting elongated nucleic acid.

29 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module determines a recombination frequency or a length, or both a recombination frequency and a length, for the resulting elongated nucleic acids.

30 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length by detecting incorporation of one or more labeled nucleic acid or nucleotide into the resulting elongated nucleic acid.

31 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length by detecting one or more label associated with the resulting elongated nucleic acid.

32 (AMENDED). The device or **[integrated]** system of claim 30, wherein the label is a dye, radioactive label, biotin, digoxin, or a fluorophore.

33 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length with a fluorogenic 5' nuclease assay.

34 (AMENDED). The device or **[integrated]** system of claim 1, wherein the physical or logical array of reaction mixtures is incorporated into a microscale device, or wherein at least one of the reaction mixtures is incorporated into a microscale device, or wherein the one or more shuffled or mutagenized nucleic acids or the one or more transcribed shuffled or mutagenized nucleic acids is found within a microscale device, or wherein the one or more in vitro translation reagents is found within a microscale device.

35 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module comprises one or more microscale channel through which a shuffling reagent or product is flowed.

36 (AMENDED). The device or **[integrated]** system of claim 35, wherein the channel is integrated in a chip.

37 (AMENDED). The device or **[integrated]** system of claim 35, wherein liquid flow through the device is mediated by capillary flow, differential pressure between one or more inlets and outlets, electroosmosis, hydraulic or mechanical pressure, or peristalsis.

38 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid fragments are contacted in a single pool.

39 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid fragments are contacted in multiple pools.

40 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more multiwell plates, or onto one or more solid substrates, or into one or more microscale systems, or into one or more containers.

41 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module pre-dilutes the resulting elongated nucleic acids and dispenses them into one or more multiwell plates.

42 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more multiwell plates at a selected density per well of the elongated nucleic acids.

43 (AMENDED). The device or **[integrated]** system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more master multiwell plates and PCR amplifies the resulting master array of elongated nucleic acids to produce an amplified array of elongated nucleic acids, the shuffling module further comprising a array copy system which transfers aliquots from the wells of the one or more master multiwell plates to one or more copy multiwell plates.

44 (AMENDED). The device or **[integrated]** system of claim 43, wherein an extent of PCR amplification is determined by one or more technique selected from: an incorporation of a label into one or more amplified elongated nucleic acid, and a fluorogenic 5' nuclease assay.

45 (AMENDED). The device or **[integrated]** system of claim 43, wherein the array of reaction mixtures is formed by separate or simultaneous addition of an in vitro transcription reagent and an in vitro translation reagent to the one or more copy multiwell

plates, or to a duplicate set thereof, wherein the elongated nucleic acids comprise the one or more shuffled nucleic acids.

46 (AMENDED). The device or **[integrated]** system of claim 1, further comprising one or more sources of one or more nucleic acids, the one or more sources collectively or individually comprising a first population of nucleic acids, wherein the shuffled nucleic acids are produced by recombining the one or more members of the first population of nucleic acids.

47 (AMENDED). The device or **[integrated]** system of claim 46, the one or more sources of nucleic acids comprising at least one nucleic acid selected from: a synthetic nucleic acid, a DNA, an RNA, a DNA analogue, an RNA analogue, a genomic DNA, a cDNA, an mRNA, a DNA generated by reverse transcription, an nRNA, an aptamer, a polysome associated nucleic acid, a cloned nucleic acid, a cloned DNA, a cloned RNA, a plasmid DNA, a phagemid DNA, a viral DNA, a viral RNA, a YAC DNA, a cosmid DNA, a fosmid DNA, a BAC DNA, a P1-mid, a phage DNA, a single-stranded DNA, a double-stranded DNA, a branched DNA, a catalytic nucleic acid, an antisense nucleic acid, an in vitro amplified nucleic acid, a PCR amplified nucleic acid, an LCR amplified nucleic acid, a Q∃-replicase amplified nucleic acid, an oligonucleotide, a nucleic acid fragment, a restriction fragment and a combination thereof.

48 (AMENDED). The device or **[integrated]** system of claim 46, further comprising a population destination region, wherein, during operation of the device, one or more members of the first population are moved from the one or more sources of the one or more nucleic acids to the one or more destination regions.

49 (AMENDED). The device or **[integrated]** system of claim 48, further comprising nucleic acid movement means for moving the one or more members from the one or more sources of the one or more nucleic acids to the one or more destination regions.

50 (AMENDED). The device or **[integrated]** system of claim 46, 48, or 49 further comprising a source of an in vitro transcription reagent or an in vitro translation reagent,

wherein, during operation of the device, the in vitro transcription reagent or an in vitro translation reagent is flowed into contact with the members of the first population.

51 (AMENDED). The device of claim 50, wherein the members of the first population are fixed at the one or more sources of one or more nucleic acids or at the one or more destination regions.

52 (AMENDED). The device or **[integrated]** system of claim 49, wherein the nucleic acid movement means comprises one or more movement means selected from: a fluid pressure modulator, an electrokinetic fluid force modulator, a thermokinetic modulator, a capillary flow mechanism, a centrifugal force modulator, a robotic armature, a pipettor, a conveyor mechanism, a peristaltic pump or mechanism, a magnetic field generator, an electric field generator, and one or more fluid flow path.

53 (AMENDED). The device or **[integrated]** system of claim 48, the one or more sources of nucleic acids, or the one or more population destination regions comprising one or more member selected from: a solid phase array, a liquid phase array, a container, a microtiter tray, a microtiter tray well, a microfluidic component, a microfluidic chip, a test tube, a centrifugal rotor, a microscope slide, an organism, a cell, a tissue, a liposome, a detergent particle, and a combination thereof.

54 (AMENDED). The device or **[integrated]** system of claim 45, wherein, during operation of the device, the first population of nucleic acids is arranged into one or more physical or logical recombinant nucleic acid arrays.

55 (AMENDED). The device or **[integrated]** system of claim 54, further comprising a duplicate of at least one of the one or more physical or logical recombinant nucleic acid arrays.

56 (AMENDED). The device or **[integrated]** system of claim 45 or 54, further comprising one or more recombination modules which move one or more members of the first population of nucleic acids into contact with one another, thereby facilitating recombination of the first population of nucleic acids.

57 (AMENDED). The device or **[integrated]** system of claim 1, further comprising one or more reaction mixture arraying modules, which arraying modules move one or more of the one or more shuffled nucleic acids or the one or more transcribed shuffled nucleic acids or the in vitro translation reactant components into one or more spatial positions, thereby placing the one or more shuffled nucleic acids or the one or more transcribed shuffled nucleic acids or the in vitro translation reactant component into locations in the array of reaction mixtures.

58 (AMENDED). The device of **[integrated]** system of claim 1, further comprising a shuffled nucleic acid master array, which master array physically or logically corresponds to positions of the shuffled nucleic acids in the reaction mixture array.

59 (AMENDED). The device or **[integrated]** system of claim 58, further comprising a nucleic acid amplification module, which module amplifies members of the shuffled nucleic acid master array, or a duplicate thereof.

60 (AMENDED). The device or **[integrated]** system of claim 59, the amplification module comprising a heating or cooling element.

61 (AMENDED). The device or **[integrated]** system of claim 59, the amplification module comprising a DNA micro-amplifier.

62 (AMENDED). The device or **[integrated]** system of claim 59, the amplification module comprising a DNA micro-amplifier, the micro-amplifier comprising one or more of: a programmable resistor, a micromachined zone heating chemical amplifier, a Peltier solid state heat pump, a heat pump, a heat exchanger, a hot air blower, a resistive heater, a refrigeration unit, a heat sink, or a Joule Thompson cooling device.

63 (AMENDED). The device or **[integrated]** system of claim 59, further comprising a duplicate amplified array, which duplicate amplified array comprises amplicons of the nucleic acid master array, or a duplicate thereof.

64 (AMENDED). The device or **[integrated]** system of claim 58, wherein, during operation of the device, the array of reaction mixtures produces an array of reaction

mixture products, the device or **[integrated]** system further comprising one or more product identification or purification modules, which product identification modules identify one or more members of the array of reaction products.

65 (AMENDED). The device or **[integrated]** system of claim 64, wherein the product identification or purification modules comprise one or more of: a gel, a polymeric solution, a liposome, a microemulsion, a microdroplet, an affinity matrix, a plasmon resonance detector, a BIACORE, a GC detector, an ultraviolet or visible light sensor, an epifluorescence detector, a fluorescence detector, a fluorescent array, a CCD, a digital imager, a scanner, a confocal imaging device, an optical sensor, a FACS detector, a micro-FACS unit, a temperature sensor, a mass spectrometer, a stereo-specific product detector, an Elisa reagent, an enzyme, an enzyme substrate an antibody, an antigen, a refractive index detector, a polarimeter, a pH detector, a pH-stat device, an ion selective sensor, a calorimeter, a film, a radiation sensor, a Geiger counter, a scintillation counter, a particle counter, an H_2O_2 detection system, an electrochemical sensor, ion/gas selective electrodes, and capillary electrophoresis.

66 (AMENDED). The device or **[integrated]** system of claim 64, wherein the one or more reaction product array members are moved into proximity to the product identification module, or wherein the product identification module performs an xyz translation, thereby moving the product identification module proximal to the array of reaction products.

67 (AMENDED). The device or **[integrated]** system of claim 66, wherein the one or more reaction product array members are flowed into proximity to the product identification module, wherein an in-line purification system purifies the one or more reaction product array members from associated materials.

68 (AMENDED). The device or **[integrated]** system of claim 64, wherein the reaction products comprise one or more polypeptide, one or more nucleic acid, one or more catalytic RNA, or one or more biologically active RNA.

69 (AMENDED). The device or **[integrated]** system of claim 68, wherein the one or more catalytic RNA is a ribozyme, or wherein the biologically active RNA is an anti-sense RNA.

70 (AMENDED). The device or **[integrated]** system of claim 68, wherein the device further comprises a source of one or more lipid, which one or more lipid is flowed into contact with the one or more polypeptide, or wherein the lipid is flowed into contact with the physical or logical array of reaction mixtures, or wherein the lipid is flowed into contact with the one or more transcribed shuffled or mutagenized nucleic acids, thereby producing one or more liposomes or micelles comprising the polypeptide, reaction mixture components, or one or more transcribed shuffled or mutagenized nucleic acids.

71 (AMENDED). The device or **[integrated]** system of claim 64, wherein the reaction products comprise one or more polypeptide and wherein the device further comprises one or more protein refolding reagent, which refolding reagent is flowed into contact with the one or more polypeptide.

72 (AMENDED). The device or **[integrated]** system of claim 71, wherein the refolding reagent comprises one or more of: guanidine, guanidinium, urea, a detergent, a chelating agent, DTT, DTE, or a chaperonin.

73 (AMENDED). The device or **[integrated]** system of claim 64, the product identification or purification modules comprising one or more of: a protein detector, or protein purification means.

74 (AMENDED). The device or **[integrated]** system of claim 64, the product identification or purification modules comprising an instruction set for discriminating between members of the array of reaction products based upon one or more of: a physical characteristic of the members, an activity of the members, or concentrations of the members.

75 (AMENDED). The device or **[integrated]** system of claim 64, further comprising a secondary product array produced by re-arraying members of the reaction product array

such that the secondary product array has a selected concentration of product members in the secondary product array.

76 (AMENDED). The device or **[integrated]** system of claim 75, wherein the selected concentration is approximately the same for a plurality of product members in the secondary product array.

77 (AMENDED). The device or **[integrated]** system of claim 64, further comprising an instruction set for determining a correction factor which accounts for variation in polypeptide concentration at different positions in the amplified physical or logical array of polypeptides.

78 (AMENDED). The device or **[integrated]** system of claim 64 or 75, further comprising a substrate addition module which substrate addition module adds one or more substrate to a plurality of members of the product array or the secondary product array.

79 (AMENDED). The device or system of claim 78, further comprising a substrate conversion detector which monitors formation of a product produced by contact between the one or more substrate and one or more of the plurality of members of the product array or the secondary product array.

80 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored indirectly.

81 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored by monitoring loss of the substrate over time.

82 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored enantioselectively, regioselectively or stereo selectively.

83 (AMENDED). The device or system of claim 82, wherein formation of the product or disappearance of substrate is monitored by adding at least one isomer, enantiomer or

stereoismer in substantially pure form, which substantially pure form is independent of other potential isomers.

84 (AMENDED). The device or system of claim 79, wherein formation of the product is monitored by detecting formation of peroxide, protons, or halides, or reduced or oxidized cofactors.

85 (AMENDED). The device or system of claim 79, wherein formation of the product is monitored by detecting changes in heat or entropy which result from contact between the substrate and the product, or by detecting changes in mass, charge, fluorescence, epifluorescence, by chromatography, luminescence or absorbance, of the substrate or the product, which result from contact between the substrate and the product.

86 (AMENDED). The device or **[integrated]** system of claim 64, the device or **[integrated]** system further comprising an array correspondence module, which array correspondence module identifies, determines or records the location of an identified product in the array of reaction mixture products which is identified by the one or more product identification modules, or which array correspondence module determines or records the location of at least a first nucleic acid member of the shuffled nucleic acid master array, or a duplicate thereof, or of an amplified duplicate array, which member corresponds to the location of one or more member of the array of reaction products.

87 (AMENDED). The device or **[integrated]** system of claim 73, further comprising one or more secondary selection module, which secondary selection module selects at least the first member for further recombination, which selection is based upon the location of a product identified by the product identification modules.

88 (AMENDED). The device or **[integrated]** system of claim 64, further comprising a screening or selection module, the module comprising one or more of:

an array reader, which reader detects one or more member of the array of reaction products;

an enzyme which converts one or more member of the array of reaction products into one or more detectable products;

a substrate which is converted by the one or more member of the array of reaction products into one or more detectable products;

a cell which produces a detectable signal upon incubation with the one or more member of the array of reaction products;

a reporter gene which is induced by one or more member of the array of reaction products;

a promoter which is induced by one or more member of the array of reaction products, which promoter directs expression of one or more detectable products; or

an enzyme or receptor cascade which is induced by the one or more member of the array of reaction products.

89 (AMENDED). The device or **[integrated]** system of claim 87, further comprising a secondary recombination module, which module physically contacts the first member, or an amplicon thereof, to an additional member of the shuffled nucleic acid master array, or the duplicate thereof, or the amplified duplicate array, thereby permitting physical recombination between the first and additional members.

90 (AMENDED). The device or **[integrated]** system of claim 1, further comprising a DNA fragmentation module and a recombination region, which DNA fragmentation module comprises one or more of: a nuclease, a mechanical shearing device, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, a chemical nucleic acid chain terminator, or an oligonucleotide synthesizer, wherein, during operation of the device, fragmented DNAs produced in the DNA fragmentation module are recombined in the recombination region to produce the one or more shuffled nucleic acids.

91 (AMENDED). The device or **[integrated]** system of claim 1, further comprising a module which performs one or more of: error prone PCR, site saturation mutagenesis, or site-directed mutagenesis.

92 (AMENDED). The device or **[integrated]** system of claim 1, further comprising a data structure embodied in a computer, an analog computer, a digital computer, or a

computer readable medium, which data structure corresponds to the one or more shuffled nucleic acids.

93 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more reaction mixtures comprise one or more shuffled nucleic acids arranged in a microtiter tray at an average of approximately 0.1-100 shuffled nucleic acids per well.

94 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more reaction mixtures comprise one or more shuffled nucleic acids arranged in a microtiter tray at an average of approximately 1-5 shuffled nucleic acids per well.

95 (AMENDED). The device or **[integrated]** system of claim 1, further comprising a diluter, which diluter pre-dilutes the concentration of the one or more shuffled or mutated nucleic acids prior to addition of the shuffled or mutant nucleic acids to the reaction mixtures.

96 (AMENDED). The device or **[integrated]** system of claim 95, wherein the concentration of the one or more shuffled nucleic acids is about 0.01 to 100 molecules per microliter.

97 (AMENDED). The device or **[integrated]** system of claim 1, wherein the reaction mixtures are produced by adding the in vitro translation reactant and, optionally, an in vitro transcription reagents, to a duplicate shuffled or mutated nucleic acid array, which duplicate shuffled or mutated nucleic acid array is duplicated from a master array of the shuffled or mutated nucleic acids produced by spatially or logically separating members of a population of the shuffled or mutated nucleic acids to produce a physical or logical array of the shuffled or mutated nucleic acids, by one or more arraying technique selected from:

(i) lyophilizing members of the population of shuffled nucleic acids on a solid surface, thereby forming a solid phase array;

(ii) chemically coupling members of the population of shuffled nucleic acids to a solid surface, thereby forming a solid phase array;

(iii) rehydrating members of the population of shuffled nucleic acids on a solid surface, thereby forming a liquid phase array;

(iv) cleaving chemically coupled members of the population of shuffled nucleic acids from a solid surface, thereby forming a liquid phase array;

(v) accessing one or more physically separated logical array members from one or more sources of shuffled nucleic acids and flowing the physically separated logical array members to one or more destination, the one or more destinations constituting a logical array of the shuffled nucleic acids; and,

(vi) printing members of a population of shuffled nucleic acids onto a solid material to form a solid phase array.

98 (AMENDED). The device or **[integrated]** system of claim 1, wherein the one or more shuffled nucleic acids are produced by synthesizing a set of overlapping oligonucleotides, or by cleaving a plurality of homologous nucleic acids to produce a set of cleaved homologous nucleic acids, or both, and permitting recombination to occur between the set of overlapping oligonucleotides, the set of cleaved homologous nucleic acids, or both the set of overlapping oligonucleotides and the set of cleaved homologous nucleic acids.

99 (AMENDED). The device or **[integrated]** system of claim 1, wherein greater than about 1% of the physical or logical array of reaction mixtures comprise shuffled or mutant nucleic acids having one or more base changes relative to a parental nucleic acid.

APPENDIX B

CLAIMS PENDING IN USSN 09/760,010 WITH ENTRY OF THIS AMENDMENT

1 (AMENDED). A device or system, comprising: a physical or logical array of reaction mixtures, each reaction mixture comprising one or more shuffled or mutagenized nucleic acids or one or more transcribed shuffled or transcribed mutagenized nucleic acids and one or more in vitro translation reagents.

2 (AMENDED). The device or system of claim 1, further comprising a duplicate of the physical or logical array.

3 (AMENDED). The device or system of claim 1, further comprising a bar-code based sample tracking module, which module comprises a bar code reader and a computer readable database comprising at least one entry for at least one array or at least one array member, which entry is corresponded to at least one bar code.

4 (AMENDED). The device or system of claim 1, further a long term storage device comprising of one or more of: a refrigerator; an electrically powered cooling device; a device capable of maintaining a temperature of < 0 C; a freezer; a device which uses liquid nitrogen or liquid helium for cooling storing or freezing samples, a container comprising wet or dry ice, a constant temperature and/or constant humidity chamber or incubator; or an automated sample storage or retrieval unit.

5 (AMENDED). The device or system of claim 4, further comprising one or more modules for moving arrays or array members into the long term storage device.

6 (AMENDED). The device or system of claim 1, further comprising a copy array comprising a copy of each of a plurality of members of the one or more shuffled or mutagenized nucleic acids in a physically or logically accessible arrangement of the members.

7 (AMENDED). The device or system of claim 1, wherein a plurality of the reaction mixtures further comprise one or more translation products or one or more transcription products, or both one or more translation products and one or more transcription products.

8 (AMENDED). The device or system of claim 1, wherein the array of reaction mixtures comprises a solid phase, liquid phase or mixed phase array of one or more of: the one or more shuffled nucleic acids, the one or more transcribed shuffled nucleic acids, or the one or more in vitro translation reagents.

9 (AMENDED). The device or system of claim 1, wherein the one or more shuffled nucleic acids are homologous.

10 (AMENDED). The device or system of claim 1, wherein the one or more transcribed shuffled nucleic acid is an mRNA.

11 (AMENDED). The device or system of claim 1, wherein the one or more in vitro translation reagents comprise one or more of: a reticulocyte lysate, a rabbit reticulocyte lysate, a canine microsome translation mixture, a wheat germ in vitro translation (IVT) mixture, or an *E coli* lysate.

12 (AMENDED). The device or system of claim 1, further comprising one or more in vitro transcription reagents.

13 (AMENDED). The device or system of claim 12, wherein the in vitro transcription reagents comprises one or more of: an *E. coli* lysate, an *E. coli* extract, an *E coli* s20 extract, a canine microsome system, a HeLa nuclear extract in vitro transcription component, an SP6 polymerase, a T3 polymerase or a T7 RNA polymerase

14 (AMENDED). The device or system of claim 1, further comprising a nucleic acid shuffling or mutagenesis module, which nucleic acid shuffling or mutagenesis module accepts input nucleic acids or character strings corresponding to input nucleic acids and manipulates the input nucleic acids or the character strings corresponding to input nucleic

acids to produce output nucleic acids, which output nucleic acids comprise the one or more shuffled or mutagenized nucleic acids in the reaction mixture array.

15 (AMENDED). The device or system of claim 14, wherein the output nucleic acids comprise one or more sequence which controls transcription or translation.

16 (AMENDED). The device or system of claim 14, wherein the nucleic acid shuffling or mutagenesis module comprises a DNA shuffling module, which DNA module accepts input DNAs or character strings corresponding to input DNAs and manipulates the input DNAs or the character strings corresponding to input DNAs to produce output DNAs, which output DNAs comprise the one or more shuffled DNAs in the reaction mixture array.

17 (AMENDED). The device or system of claim 1, wherein the nucleic acid shuffling or mutagenesis module is preceded by a module which allows overlapping synthetic oligonucleotides to be first assembled into oligonucleotide multimers or functional open reading frames prior to entering the mutagenesis or shuffling module.

18 (AMENDED). The device or system of claim 14, wherein one or more module comprises or is operatively linked to a thermocycling device.

19 (AMENDED). The device or system of claim 14, wherein the nucleic acid shuffling or mutagenesis module comprises a mutagenesis module, which mutagenesis module mutagenizes the DNA.

20 (AMENDED). The device or system of claim 14, wherein the nucleic acid shuffling or mutagenesis module fragments the input nucleic acids to produce nucleic acid fragments, or wherein the input nucleic acids comprises cleaved or synthetic nucleic acid fragments.

21 (AMENDED). The device or system of claim 14, wherein the shuffling or mutagenesis module is mechanically, electronically, robotically or fluidically coupled to at least one other array operation module.

22 (AMENDED). The device or system of claim 14, wherein, the nucleic acid shuffling or mutagenesis module performs one or more of: StEP PCR, uracil incorporation or chain termination.

23 (AMENDED). The device or system of claim 14, or 20, wherein the nucleic acid shuffling module comprises an identification portion, which identification portion identifies one or more nucleic acid portion or subportion.

24 (AMENDED). The device or system of claim 14 or 20, wherein the nucleic acid shuffling module comprises a fragment length purification portion, which fragment length purification portion purifies selected length fragments of the nucleic acid fragments.

25 (AMENDED). The device or system of claim 20, wherein the nucleic acid shuffling module permits hybridization of the nucleic acid fragments and wherein the nucleic acid shuffling module comprises a polymerase which elongates the hybridized nucleic acid.

26 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module combines one or more translation or transcription control sequence into the resulting elongated nucleic acid.

27 (AMENDED). The device or system of claim 26, wherein the one or more translation or transcription control sequence is combined into the resulting elongated nucleic acid using the polymerase, or a ligase, or both the polymerase and the ligase.

28 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module separates, identifies, purifies or immobilizes the resulting elongated nucleic acid.

29 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module determines a recombination frequency or a length, or both a recombination frequency and a length, for the resulting elongated nucleic acids.

30 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length by detecting incorporation of one or more labeled nucleic acid or nucleotide into the resulting elongated nucleic acid.

31 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length by detecting one or more label associated with the resulting elongated nucleic acid.

32 (AMENDED). The device or system of claim 30, wherein the label is a dye, radioactive label, biotin, digoxin, or a fluorophore.

33 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module determines nucleic acid length with a fluorogenic 5' nuclease assay.

34 (AMENDED). The device or system of claim 1, wherein the physical or logical array of reaction mixtures is incorporated into a microscale device, or wherein at least one of the reaction mixtures is incorporated into a microscale device, or wherein the one or more shuffled or mutagenized nucleic acids or the one or more transcribed shuffled or mutagenized nucleic acids is found within a microscale device, or wherein the one or more in vitro translation reagents is found within a microscale device.

35 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module comprises one or more microscale channel through which a shuffling reagent or product is flowed.

36 (AMENDED). The device or system of claim 35, wherein the channel is integrated in a chip.

37 (AMENDED). The device or system of claim 35, wherein liquid flow through the device is mediated by capillary flow, differential pressure between one or more inlets and outlets, electroosmosis, hydraulic or mechanical pressure, or peristalsis.

38 (AMENDED). The device or system of claim 25, wherein the nucleic acid fragments are contacted in a single pool.

39 (AMENDED). The device or system of claim 25, wherein the nucleic acid fragments are contacted in multiple pools.

40 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more multiwell plates, or onto one or more solid substrates, or into one or more microscale systems, or into one or more containers.

41 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module pre-dilutes the resulting elongated nucleic acids and dispenses them into one or more multiwell plates.

42 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more multiwell plates at a selected density per well of the elongated nucleic acids.

43 (AMENDED). The device or system of claim 25, wherein the nucleic acid shuffling module dispenses the resulting elongated nucleic acids into one or more master multiwell plates and PCR amplifies the resulting master array of elongated nucleic acids to produce an amplified array of elongated nucleic acids, the shuffling module further comprising a array copy system which transfers aliquots from the wells of the one or more master multiwell plates to one or more copy multiwell plates.

44 (AMENDED). The device or system of claim 43, wherein an extent of PCR amplification is determined by one or more technique selected from: an incorporation of a label into one or more amplified elongated nucleic acid, and a fluorogenic 5' nuclease assay.

45 (AMENDED). The device or system of claim 43, wherein the array of reaction mixtures is formed by separate or simultaneous addition of an in vitro transcription reagent and an in vitro translation reagent to the one or more copy multiwell plates, or to a duplicate set thereof, wherein the elongated nucleic acids comprise the one or more shuffled nucleic acids.

46 (AMENDED). The device or system of claim 1, further comprising one or more sources of one or more nucleic acids, the one or more sources collectively or individually comprising a first population of nucleic acids, wherein the shuffled nucleic acids are produced by recombining the one or more members of the first population of nucleic acids.

47 (AMENDED). The device or system of claim 46, the one or more sources of nucleic acids comprising at least one nucleic acid selected from: a synthetic nucleic acid, a DNA, an RNA, a DNA analogue, an RNA analogue, a genomic DNA, a cDNA, an mRNA, a DNA generated by reverse transcription, an nRNA, an aptamer, a polysome associated nucleic acid, a cloned nucleic acid, a cloned DNA, a cloned RNA, a plasmid DNA, a phagemid DNA, a viral DNA, a viral RNA, a YAC DNA, a cosmid DNA, a fosmid DNA, a BAC DNA, a P1-mid, a phage DNA, a single-stranded DNA, a double-stranded DNA, a branched DNA, a catalytic nucleic acid, an antisense nucleic acid, an in vitro amplified nucleic acid, a PCR amplified nucleic acid, an LCR amplified nucleic acid, a Q∃-replicase amplified nucleic acid, an oligonucleotide, a nucleic acid fragment, a restriction fragment and a combination thereof.

48 (AMENDED). The device or system of claim 46, further comprising a population destination region, wherein, during operation of the device, one or more members of the first population are moved from the one or more sources of the one or more nucleic acids to the one or more destination regions.

49 (AMENDED). The device or system of claim 48, further comprising nucleic acid movement means for moving the one or more members from the one or more sources of the one or more nucleic acids to the one or more destination regions.

50 (AMENDED). The device or system of claim 46, 48, or 49 further comprising a source of an in vitro transcription reagent or an in vitro translation reagent, wherein, during operation of the device, the in vitro transcription reagent or an in vitro translation reagent is flowed into contact with the members of the first population.

51 (AMENDED). The device of claim 50, wherein the members of the first population are fixed at the one or more sources of one or more nucleic acids or at the one or more destination regions.

52 (AMENDED). The device or system of claim 49, wherein the nucleic acid movement means comprises one or more movement means selected from: a fluid pressure modulator, an electrokinetic fluid force modulator, a thermokinetic modulator, a capillary flow mechanism, a centrifugal force modulator, a robotic armature, a pipettor, a conveyor mechanism, a peristaltic pump or mechanism, a magnetic field generator, an electric field generator, and one or more fluid flow path.

53 (AMENDED). The device or system of claim 48, the one or more sources of nucleic acids, or the one or more population destination regions comprising one or more member selected from: a solid phase array, a liquid phase array, a container, a microtiter tray, a microtiter tray well, a microfluidic component, a microfluidic chip, a test tube, a centrifugal rotor, a microscope slide, an organism, a cell, a tissue, a liposome, a detergent particle, and a combination thereof.

54 (AMENDED). The device or system of claim 45, wherein, during operation of the device, the first population of nucleic acids is arranged into one or more physical or logical recombinant nucleic acid arrays.

55 (AMENDED). The device or system of claim 54, further comprising a duplicate of at least one of the one or more physical or logical recombinant nucleic acid arrays.

56 (AMENDED). The device or system of claim 45 or 54, further comprising one or more recombination modules which move one or more members of the first population of nucleic acids into contact with one another, thereby facilitating recombination of the first population of nucleic acids.

57 (AMENDED). The device or system of claim 1, further comprising one or more reaction mixture arraying modules, which arraying modules move one or more of the one or more shuffled nucleic acids or the one or more transcribed shuffled nucleic acids or the

in vitro translation reactant components into one or more spatial positions, thereby placing the one or more shuffled nucleic acids or the one or more transcribed shuffled nucleic acids or the in vitro translation reactant component into locations in the array of reaction mixtures.

58 (AMENDED). The device of system of claim 1, further comprising a shuffled nucleic acid master array, which master array physically or logically corresponds to positions of the shuffled nucleic acids in the reaction mixture array.

59 (AMENDED). The device or system of claim 58, further comprising a nucleic acid amplification module, which module amplifies members of the shuffled nucleic acid master array, or a duplicate thereof.

60 (AMENDED). The device or system of claim 59, the amplification module comprising a heating or cooling element.

61 (AMENDED). The device or system of claim 59, the amplification module comprising a DNA micro-amplifier.

62 (AMENDED). The device or system of claim 59, the amplification module comprising a DNA micro-amplifier, the micro-amplifier comprising one or more of: a programmable resistor, a micromachined zone heating chemical amplifier, a Peltier solid state heat pump, a heat pump, a heat exchanger, a hot air blower, a resistive heater, a refrigeration unit, a heat sink, or a Joule Thompson cooling device.

63 (AMENDED). The device or system of claim 59, further comprising a duplicate amplified array, which duplicate amplified array comprises amplicons of the nucleic acid master array, or a duplicate thereof.

64 (AMENDED). The device or system of claim 58, wherein, during operation of the device, the array of reaction mixtures produces an array of reaction mixture products, the device or **[integrated]** system further comprising one or more product identification or purification modules, which product identification modules identify one or more members of the array of reaction products.

65 (AMENDED). The device or system of claim 64, wherein the product identification or purification modules comprise one or more of: a gel, a polymeric solution, a liposome, a microemulsion, a microdroplet, an affinity matrix, a plasmon resonance detector, a BIACORE, a GC detector, an ultraviolet or visible light sensor, an epifluorescence detector, a fluorescence detector, a fluorescent array, a CCD, a digital imager, a scanner, a confocal imaging device, an optical sensor, a FACS detector, a micro-FACS unit, a temperature sensor, a mass spectrometer, a stereo-specific product detector, an Elisa reagent, an enzyme, an enzyme substrate an antibody, an antigen, a refractive index detector, a polarimeter, a pH detector, a pH-stat device, an ion selective sensor, a calorimeter, a film, a radiation sensor, a Geiger counter, a scintillation counter, a particle counter, an H_2O_2 detection system, an electrochemical sensor, ion/gas selective electrodes, and capillary electrophoresis.

66 (AMENDED). The device or system of claim 64, wherein the one or more reaction product array members are moved into proximity to the product identification module, or wherein the product identification module performs an xyz translation, thereby moving the product identification module proximal to the array of reaction products.

67 (AMENDED). The device or system of claim 66, wherein the one or more reaction product array members are flowed into proximity to the product identification module, wherein an in-line purification system purifies the one or more reaction product array members from associated materials.

68 (AMENDED). The device or system of claim 64, wherein the reaction products comprise one or more polypeptide, one or more nucleic acid, one or more catalytic RNA, or one or more biologically active RNA.

69 (AMENDED). The device or system of claim 68, wherein the one or more catalytic RNA is a ribozyme, or wherein the biologically active RNA is an anti-sense RNA.

70 (AMENDED). The device or system of claim 68, wherein the device further comprises a source of one or more lipid, which one or more lipid is flowed into contact with the one or more polypeptide, or wherein the lipid is flowed into contact with the

physical or logical array of reaction mixtures, or wherein the lipid is flowed into contact with the one or more transcribed shuffled or mutagenized nucleic acids, thereby producing one or more liposomes or micelles comprising the polypeptide, reaction mixture components, or one or more transcribed shuffled or mutagenized nucleic acids.

71 (AMENDED). The device or system of claim 64, wherein the reaction products comprise one or more polypeptide and wherein the device further comprises one or more protein refolding reagent, which refolding reagent is flowed into contact with the one or more polypeptide.

72 (AMENDED). The device or system of claim 71, wherein the refolding reagent comprises one or more of: guanidine, guanidinium, urea, a detergent, a chelating agent, DTT, DTE, or a chaperonin.

73 (AMENDED). The device or system of claim 64, the product identification or purification modules comprising one or more of: a protein detector, or protein purification means.

74 (AMENDED). The device or system of claim 64, the product identification or purification modules comprising an instruction set for discriminating between members of the array of reaction products based upon one or more of: a physical characteristic of the members, an activity of the members, or concentrations of the members.

75 (AMENDED). The device or system of claim 64, further comprising a secondary product array produced by re-arraying members of the reaction product array such that the secondary product array has a selected concentration of product members in the secondary product array.

76 (AMENDED). The device or system of claim 75, wherein the selected concentration is approximately the same for a plurality of product members in the secondary product array.

77 (AMENDED). The device or system of claim 64, further comprising an instruction set for determining a correction factor which accounts for variation in polypeptide

concentration at different positions in the amplified physical or logical array of polypeptides.

78 (AMENDED). The device or system of claim 64 or 75, further comprising a substrate addition module which substrate addition module adds one or more substrate to a plurality of members of the product array or the secondary product array.

79 (AMENDED). The device or system of claim 78, further comprising a substrate conversion detector which monitors formation of a product produced by contact between the one or more substrate and one or more of the plurality of members of the product array or the secondary product array.

80 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored indirectly.

81 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored by monitoring loss of the substrate over time.

82 (AMENDED). The device or system of claim 79, wherein formation of the product or disappearance of substrate is monitored enantioselectively, regioselectively or stereo selectively.

83 (AMENDED). The device or system of claim 82, wherein formation of the product or disappearance of substrate is monitored by adding at least one isomer, enantiomer or stereoismer in substantially pure form, which substantially pure form is independent of other potential isomers.

84 (AMENDED). The device or system of claim 79, wherein formation of the product is monitored by detecting formation of peroxide, protons, or halides, or reduced or oxidized cofactors.

85 (AMENDED). The device or system of claim 79, wherein formation of the product is monitored by detecting changes in heat or entropy which result from contact between the substrate and the product, or by detecting changes in mass, charge, fluorescence,

epifluorescence, by chromatography, luminescence or absorbance, of the substrate or the product, which result from contact between the substrate and the product.

86 (AMENDED). The device or system of claim 64, the device or system further comprising an array correspondence module, which array correspondence module identifies, determines or records the location of an identified product in the array of reaction mixture products which is identified by the one or more product identification modules, or which array correspondence module determines or records the location of at least a first nucleic acid member of the shuffled nucleic acid master array, or a duplicate thereof, or of an amplified duplicate array, which member corresponds to the location of one or more member of the array of reaction products.

87 (AMENDED). The device or system of claim 73, further comprising one or more secondary selection module, which secondary selection module selects at least the first member for further recombination, which selection is based upon the location of a product identified by the product identification modules.

88 (AMENDED). The device or system of claim 64, further comprising a screening or selection module, the module comprising one or more of:

an array reader, which reader detects one or more member of the array of reaction products;

an enzyme which converts one or more member of the array of reaction products into one or more detectable products;

a substrate which is converted by the one or more member of the array of reaction products into one or more detectable products;

a cell which produces a detectable signal upon incubation with the one or more member of the array of reaction products;

a reporter gene which is induced by one or more member of the array of reaction products;

a promoter which is induced by one or more member of the array of reaction products, which promoter directs expression of one or more detectable products; or

an enzyme or receptor cascade which is induced by the one or more member of the array of reaction products.

89 (AMENDED). The device or system of claim 87, further comprising a secondary recombination module, which module physically contacts the first member, or an amplicon thereof, to an additional member of the shuffled nucleic acid master array, or the duplicate thereof, or the amplified duplicate array, thereby permitting physical recombination between the first and additional members.

90 (AMENDED). The device or system of claim 1, further comprising a DNA fragmentation module and a recombination region, which DNA fragmentation module comprises one or more of: a nuclease, a mechanical shearing device, a polymerase, a random primer, a directed primer, a nucleic acid cleavage reagent, a chemical nucleic acid chain terminator, or an oligonucleotide synthesizer, wherein, during operation of the device, fragmented DNAs produced in the DNA fragmentation module are recombined in the recombination region to produce the one or more shuffled nucleic acids.

91 (AMENDED). The device or system of claim 1, further comprising a module which performs one or more of: error prone PCR, site saturation mutagenesis, or site-directed mutagenesis.

92 (AMENDED). The device or system of claim 1, further comprising a data structure embodied in a computer, an analog computer, a digital computer, or a computer readable medium, which data structure corresponds to the one or more shuffled nucleic acids.

93 (AMENDED). The device or system of claim 1, wherein the one or more reaction mixtures comprise one or more shuffled nucleic acids arranged in a microtiter tray at an average of approximately 0.1-100 shuffled nucleic acids per well.

94 (AMENDED). The device or system of claim 1, wherein the one or more reaction mixtures comprise one or more shuffled nucleic acids arranged in a microtiter tray at an average of approximately 1-5 shuffled nucleic acids per well.

95 (AMENDED). The device or system of claim 1, further comprising a diluter, which diluter pre-dilutes the concentration of the one or more shuffled or mutated nucleic acids prior to addition of the shuffled or mutant nucleic acids to the reaction mixtures.

96 (AMENDED). The device or system of claim 95, wherein the concentration of the one or more shuffled nucleic acids is about 0.01 to 100 molecules per microliter.

97 (AMENDED). The device or system of claim 1, wherein the reaction mixtures are produced by adding the in vitro translation reactant and, optionally, an in vitro transcription reagents, to a duplicate shuffled or mutated nucleic acid array, which duplicate shuffled or mutated nucleic acid array is duplicated from a master array of the shuffled or mutated nucleic acids produced by spatially or logically separating members of a population of the shuffled or mutated nucleic acids to produce a physical or logical array of the shuffled or mutated nucleic acids, by one or more arraying technique selected from:

(i) lyophilizing members of the population of shuffled nucleic acids on a solid surface, thereby forming a solid phase array;

(ii) chemically coupling members of the population of shuffled nucleic acids to a solid surface, thereby forming a solid phase array;

(iii) rehydrating members of the population of shuffled nucleic acids on a solid surface, thereby forming a liquid phase array;

(iv) cleaving chemically coupled members of the population of shuffled nucleic acids from a solid surface, thereby forming a liquid phase array;

(v) accessing one or more physically separated logical array members from one or more sources of shuffled nucleic acids and flowing the physically separated logical array members to one or more destination, the one or more destinations constituting a logical array of the shuffled nucleic acids; and,

(vi) printing members of a population of shuffled nucleic acids onto a solid material to form a solid phase array.

98 (AMENDED). The device or system of claim 1, wherein the one or more shuffled nucleic acids are produced by synthesizing a set of overlapping oligonucleotides, or by

cleaving a plurality of homologous nucleic acids to produce a set of cleaved homologous nucleic acids, or both, and permitting recombination to occur between the set of overlapping oligonucleotides, the set of cleaved homologous nucleic acids, or both the set of overlapping oligonucleotides and the set of cleaved homologous nucleic acids.

99 (AMENDED). The device or system of claim 1, wherein greater than about 1% of the physical or logical array of reaction mixtures comprise shuffled or mutant nucleic acids having one or more base changes relative to a parental nucleic acid.